REMARKS

Claims 1-24 are pending in the application, with claims 9-24 being withdrawn from consideration.

Objections to the specification

The Examiner has objected to the specification with the assertion that letters have been omitted from various words. The Examiner specifically points to page 6, line 28; page 15, line 31; and page 16, line 31. Applicants traverse this objection and withdrawal thereof is respectfully requested. Applicants have carefully reviewed the portions of the specification pointed to by the Examiner and fail to find any misspelled terms or letters missing. Withdrawal of the objection or clarification thereof is therefore, respectfully requested.

Applicants further note in this regard that if the Examiner intended that definitions for terms recited at those sections of the specification were missing, the terms are adequately defined elsewhere in the specification. For example, "STxB-Z(n)-Cys" is defined at least at page 2, lines 25-28. Similarly, "Pep1" and "SPDP" are defined at least at page 14, lines 18-19 and page 20, lines 25-26 respectively.

Rejections under 35 U.S.C.§112, 1st paragraph

The specification has been "objected to" and claims 1-8 rejected under 35 U.S.C.§112, 1st paragraph for failing to provide an enabling disclosure. More specifically, the Examiner indicates that the plasmid pSU108 having SEQ ID NO:2 inserted between the Sph1 and Sa11 restriction sites, is needed to practice the present invention. Thus, compliance with the deposit requirements is needed to enable the invention.

Attached hereto is a copy of the deposit receipt and a declaration of Madame Florence Lazard, which evidence that the deposit of the plasmid was made in accordance with the Budapest Treaty. In addition, the undersigned state on behalf of the Applicant that any restriction on the deposit will be irrevocably removed upon grant of a patent from the present application. Withdrawal of the rejection and objection is respectfully requested.

Rejections under 35 U.S.C.§102(b)

Claims 1-8 have been rejected under 35 U.S.C.§102(b) as being anticipated by Haicheuer et al., J. Immunol. (2000) or Lee et al., Eur. J. Immunol. (1998), in view of Wang et al., WO 95/11998.

Haicheuer et al. is asserted to teach a construct of the B subunit of Shiga toxin that is fused to a tumor peptide. The

reference is further asserted to teach that the Shiga B subunit is acting as a carrier, which binds to glycolipid Gb3 in a receptor-dependent manner. The Examiner further asserts that because the Gb3 glycolipid is highly expressed on dendritic cells, the Shiga B subunit is an attractive vector for vaccine development. Finally, Haicheuer et al. is asserted to teach OVA, SL8, P815A and P1A as other possible peptides to fuse to the Shiga B subunit.

Lee et al. is similarly asserted to teach the fusion of the Shiga B subunit with a tumor antigen and that Shiga B targets dendritic cells and B cells, thus making it an attractive vaccine vector.

Wang et al. is relied on for teaching the addition of cysteine residues to synthetic peptides to increase solubility and facilitate binding of the peptide to a carrier.

Applicants traverse these rejections and withdrawal thereof is respectfully requested.

1) Haicheuer et al. -

"To anticipate a claim, a prior art reference must disclose every limitation of the claimed invention, either explicitly or inherently." In re Schreiber, 128 F.3d 1473, 1477, 44 USPQ2d 1429, 1431 (Fed. Cir. 1997).

As noted by the Examiner, Haicheuer et al. does disclose a

construct of the B subunit of Shiga toxin fused to a tumor peptide wherein, the Shiga B subunit acts as a vector for targeting the peptide through a receptor-dependent pathway, i.e. by binding to the glycolipid Gb3. Haicheuer et al. further discloses that alternative peptides can be fused to the Shiga B subunit, including OVA, SL8, P815A and P14A.

However, Haicheuer et al. does not disclose a universal polypeptide carrier wherein a cysteine amino acid residue is added to the Shiga toxin B subunit. As such, Haicheuer et al. fails to disclose each recited feature of the present invention and the present invention is therefore novel over the reference.

2) *Lee et al.* - Lee et al. discloses the fusion of the Shiga B subunit with the tumor antigen, Mage 1. The Shiga B subunit is reported to have the ability to target dendritic cells and B cells, and to thus target antigen to the exogenous class I-restricted pathway, making it an attractive vaccine vector. However, as with Haicheuer et al., Lee also fails to teach a universal polypeptide carrier having a cysteine amino acid residue added to the fusion product. As such, Lee et al. fails to disclose each recited feature of the present invention and the invention is therefore novel over the disclosure of Lee et al. Withdrawal of the rejection is respectfully requested.

3) Haicheuer et al. or Lee et al. combined with Wang et al. -

The Examiner bases the rejection on the teachings of Haicheuer et al. or Lee et al. combined with Wang et al., wherein Wang et al. is relied on for allegedly teaching a specific recited feature of the claimed invention, i.e. the feature of an additional Cys residue. The Examiner's reliance on a second reference for a critical recited feature of the invention, i.e. more than for simply showing the state of the art, means that the rejection for lack of novelty under 35 U.S.C. § 102(b) over Haicheuer et al. or Lee et al., is necessarily improper. However, the invention is further not obvious over the combined teachings of Haicheuer et al. or Lee et al. and Wang et al. for the reasons discussed below.

Applicants note initially that the Examiner has failed to properly support a rejection for *prima facie* obviousness. Specifically, Haicheuer et al. and Lee et al. fail to provide any suggestion or motivation for modifying the constructs to achieve the invention. It is well-settled in US case law that to support a *prima facie* obviousness rejection, the Examiner must find in the references relied upon, a suggestion or motivation to modify the teachings of the references so as to achieve the invention. For example, the Court of Appeals for the Federal Circuit stated in *Sibia Neurosciences, Inc. v. Cadus Pharmaceutical Corp.* that "there must be a showing of a suggestion or motivation to modify the

teachings of that refernce to the claimed invention in order to support the obviousness conclusion." *Sibia Neurosciences, Inc. v. Cadus Pharmaceutical Corp.*, 55 USPQ2d 1927 (Fed. Cir. 2000). Since there is no suggestion or motivation provided to modify Haicheuer et al. or Lee et al. or to combine the reference teachings with Wang et al., a *prima facie* rejection has not been established and withdrawal thereof is respectfully requested.

Applicants further note that even if the teachings of Haicheuer et al. or Lee et al. are combined with Wang et al., the invention remains unobvious. The present invention is directed to a universal polypeptide carrier for targeting to Gb3 expressing cells, wherein the carrier has the formula STxB-Z(n)-Cys, wherein "STxB" is the Shiga B subunit, "Z" is an amino acid that is devoid of a sulfhydryl group, with "n" being 0, 1 or a polypeptide, and "Cys" is a cysteine residue. There is no suggestion in Wang et al. of adding a cysteine residue to the Shiga B subunit to target molecules to Gb3 receptor expressing cells.

Wang et al. discloses "structured synthetic antigen libraries" (SSAL), which are made of related polypeptides that are synthesized simultaneously having recourse to a single peptide synthesis process. There is a brief, single disclosure in Wang et al. that cysteine residues can be added to synthetic peptides to increase

solubility and facilitate directed coupling of the peptide to a carrier. See page 20, lines 19-21.

However, Wang et al. fails to contain any working examples or provide any results/data regarding the use of a cysteine residue to facilitate directed binding of a peptide to a carrier and no carrier molecule is disclosed or discussed in Wang et al. More importantly, Wang et al. fails to disclose or suggest the binding of a peptide, through a cysteine residue, to a carrier that will target the peptide to a specific pathway via receptor binding, such as is accomplished with the present invention and the Shiga B subunit. There is no suggestion or prediction in Wang et al. as to whether a construct containing the cysteine residue would still target to the desired pathway.

In addition, Wang et al. discloses that the cysteine residues may be added to either the N-terminus or the C-terminus of the peptide to facilitate binding to the carrier. However, Wang et al. fails to teach the site of the carrier where the cysteine residue bound to the peptide can be coupled so that the carrier function will not be impaired.

It is well known that the addition of a cysteine residue may result in the formation of internal disulfide bonds, which can disrupt the final structure of the construct as well as the constructs functional properties. Wang et al. fails to provide the

necessary guidance that is needed to achieve the present invention, such that a universal carrier made from the Shiga B subunit is achieved that retains the ability to target specifically to Gb3 receptor pathways, if a cysteine residue has been added to the peptide. As such, the present invention is not obvious over the combined teachings of the references and withdrawal of the rejections is respectfully requested.

Should there be any outstanding matters that need to be resolved in the present application, the Examiner is respectfully requested to contact MaryAnne Armstrong, PhD. at the telephone number of the undersigned below, to conduct an interview in an effort to expedite prosecution in connection with the present application.

If necessary, the Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 02-2448 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17; particularly, extension of time fees.

Respectfully submitted,

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Attachments: Deposit receipt and Declaration regarding deposit